Amendments to the Specification:

Please replace title in the amended specification dated January 8 2004 with the following original title:

Manufacturing processes for ~~Se-methyl-L-selenocysteine~~ Se-alkylselenocysteine, Se-allylselenocysteine, Se-arylselenocysteine.

Please replace paragraph [0004] in the amended specification dated January 8 2004 with the following original paragraph:

[0004] The present patent describes efficient processes for the manufacture of L-Se-methyselenocysteine, D-Se-methylselenocysteine and DL-Se-methylselenocysteine: The structures of the referred materials are shown below; Using the same chemical process, manufacture of Se-alkylselenocysteine , Se-allylselenocysteine, Se-arylselenocysteine is possible.

Please delete paragraphs [0007.1] and [0007.2] appearing after paragraph [0007] on page 3 of the amended specification dated January 8 2004 .

Please replace paragraph [0011] in the amended specification dated January 8 2004 with the following original paragraph:

[0011] L-Chloroalanine methyl ester hydrochloride (IIa) was synthesized by a convenient method from the reaction of L-Serine methyl ester hydrochloride with ~~phosphorous pentachloride in chloroform solution. The method of Walsh~~ thionyl chloride in a solvent. The methods described earlier in the literature are not very convenient to use. For example, L-Serine methyl ester hydrochloride was reacted with phosphorous pentachloride in chloroform solution to give chloroalanine methyl ester hydrochloride (Walsh, C. T.; Schonbrunn, A.; Abeles, R. H.; J Biol Chem., 1971,246 (22), 6855-6866) ~~is but one way of synthesizing L-Chloroalanine methyl ester hydrochloride (IIa). Alternatively other methods could be used.~~ It is difficult to handle highly hygroscopic phosphorous pentachloride. The method described in the present patent uses more easily handled thionyl chloride. Then IIa is converted to L-Chloroalanine hydrochloride (IIb) by reaction with aqueous hydrochloric acid. L-Chloroalanine hydrochloride (IIb) could be neutralized with triethyl amine to form L-Chloroalanine (IIc). As mentioned, IIa, IIb and IIc ~~were~~ are all convenient raw materials for L-Se-methyl selenocysteine.

Please replace paragraph [0013] in the amended specification dated January 8 2004 with the following original paragraph:

[0013] We also found that hypophosphorous acid could be used to cleave Se-Se- bond of dimethyldiselenide and the sodium salt of methylselenol was formed using sodium hydroxide. The methyselenide sodium thus generated was reacted with L-chloroalanine methyl ester hydrochloride (IIa), or L-chloroalanine hydrochloride (IIb) or L-chloroalanine (IIc) to get L-Se-methylselenocysteine. In extension of the above concept, one can use a dialkyldiselenide as a starting material to generate alkylselenide anion which can react with IIa, IIb or IIc to yield L-Se-alkylselenocysteine. Similarly starting with diallyldiselenide and generating allyl selenide anion and further reacting with IIa or with IIb or with IIc, one can obtain L-Se-allylselenocysteine. These are straightforward extensions of the process patented in this application. Likewise diaryldiselenides could be used to generate arylselenol or arylselenide salts which could be used to produce Se-arylselenocysteine. In an analogous way, D-Se-methylselenocysteine (Ib) is obtained from D-Chloroalanine methyl ester hydrochloride (IIIa) or from D-Chloroalanine hydrochloride (IIIb) or from D-Chloroalanine (IIIc). These raw materials IIIa, IIIb and IIIc are obtainable from D-Serine methyl ester hydrochloride in a similar way described for the L-analogs.

Please replace paragraph [0014] in the amended specification dated January 8 2004 with the following original paragraph:

[0014] By similar processes, one can produce other D-Se-alkylselenocysteine or D-Se-allylselenocysteine or D-Se-arylselenocysteine. Similarly in an analogous way DL-Se-methylselenocysteine (Ic) is obtained from DL-Chloroalanine methyl ester hydrochloride (IVa) or from DL-Chloroalanine hydrochloride (IVb) or from DL-Chloroalanine (IVc). These raw materials are obtainable from DL-Serine methyl ester hydrochloride as described for the L-analogs.

Please replace paragraph [0015] in the amended specification dated January 8 2004 with the following original paragraph:

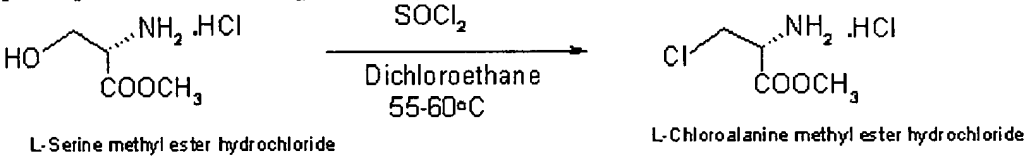
[0015] Extensions of the described processes to manufacture DL-Se-alkylselenocysteine or DL-Se-allylselenocysteine or DL-arylselenocysteine are possible.

Please replace paragraph [0016] in the amended specification dated January 8 2004 with the following original paragraph:

[0016] Additionally DL-Se-methylselenocysteine (Ic) is also obtainable from L-Se-methylselenocysteine (Ia) or from D-Se-methylselenocysteine (Ib) by raceimization as the Example 7 ~~Example 4~~ described later in this embodiment will illustrate.

Please retain paragraphs [0020], [0021], and [0022] presented in the original specification.

[0020] **Example 1 - Synthesis of L-Chloroalanine methyl ester hydrochloride:**

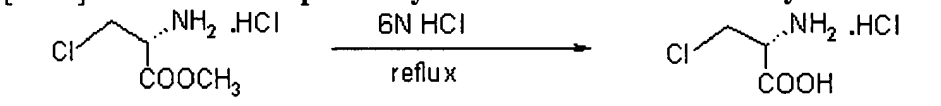


L-Serine methyl ester hydrochloride

L-Chloroalanine methyl ester hydrochloride

A 500ml RB flask was charged with L-Serine methyl ester hydrochloride (20g, 129 mmol) and dichloroethane and the resulting suspension was heated to 55°C with stirring. Thionyl chloride (30.6g, 258 mmol) was added drop wise, with vigorous stirring of the mixture. The colorless suspension turned into thick white gel during 30 minutes which became a clear yellow solution after next 30-40 minutes. Pale yellow solid started coming out of the clear solution within 10-15 minutes, ultimately making the reaction mixture as thick solid which was kept at 55°C for further 3 hours. The reaction mixture was cooled, transferred to a Buchner flask/funnel set up and using (water) vacuum all the solvent was sucked off to obtain a dry slightly yellow colored solid, which was taken to next step directly without further purification. Yield: 22g (crude weight); Melting point: 153-155°C (dec.); TLC analysis: n-Butanol:Water:Acetic acid (6:2:2); Proton NMR of the product was satisfactory.

[0021] **Example 2 - Synthesis of Chloroalanine hydrochloride:**



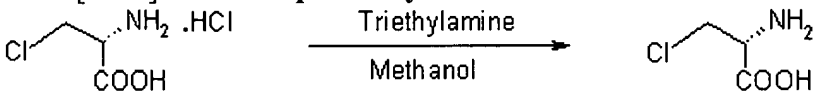
L-Chloroalanine methyl ester hydrochloride

L-Chloroalanine hydrochloride

L-Chloroalanine methyl ester hydrochloride (21 g) was dissolved in 6N hydrochloric acid and refluxed for 4 hours.

All the solvent was removed on a rotary evaporator at 90°C. To the residue obtained, 4ml of toluene was added and again evaporated to dryness. To the slightly gray colored solid, 75ml of isopropanol was added and stirred for 3 hours, cooled for 3 hours, filtered and dried in the oven for 2 hours at 60-70°C.Yield: 15g (76% from L-serine methyl ester hydrochloride); Melting point: 191-192°C (dec.)TLC analysis: n-Butanol: Water: Acetic acid (6:2:2).

[0022] **Example 3 - Synthesis of L-Chloroalanine:**

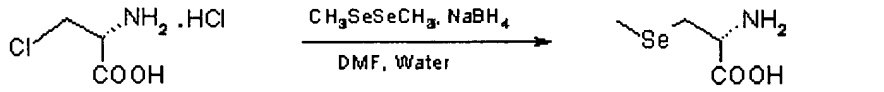


L-Chloroalanine hydrochloride — L-Chloroalanine

L-Chloroalanine hydrochloride (10g) was dissolved in methanol and triethylamine was added drop wise at room temperature and pH of the reaction mixture was adjusted to 6. After stirring for 2 hours at room temperature, the precipitated L-chloroalanine was filtered, washed with 50ml methanol and dried. Yield: 7g (90%); Melting point: 164-165°-C;TLC analysis: n-Butanol: Water: Acetic acid (6:2:2) $[\alpha]_D$: -16.28 (c 5.00, water); Chiral HPLC showed that the material obtained was only L-form.

Please replace paragraph [0023] presented in the amended specification dated January 8 2004 with the following original paragraph:

[0023] **<u>Example 4</u>** ~~**Example 1**~~ **L-Se-Methyl Selenocysteine from L-Chloroalanine hydrochloride**



L-Chloroalanine hydrochloride — L-Se-Methylselenocysteine

Dimethyldiselenide (50 g) in DMF (20 ml) was taken to get a clear solution. NaOH solution (24g in 100 ml water) was added under stirring. The mass was cooled to 5-10°C

and to this was added, portion-wise, solid sodium borohydride (6g) at < 10 °C. The reaction mixture was warmed to 40-45 ° C and maintained for 2 hrs to get a clear colorless solution.

Please replace paragraph [0028] presented in the amended specification dated January 8 2004 with the following original paragraph:

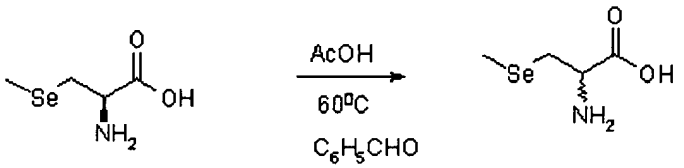
[0028] **Example 5 ~~Example 2~~ L-Se-Methyl Selenocysteine from L-Chloroalanine methyl ester hydrochloride:** Dimethyldiselenide (56 g) in DMF (25 ml) was taken to get a clear solution. NaOH solution (34g in 150 ml water) was added under stirring. The mass was cooled to 5-10°C and to this was added, portionwise, solid sodium borohydride (7g) at < 10 °C over a period of 1 hr. The reaction mixture was warmed to 40-45 °C and maintained for 2 hrs to get a clear colorless solution.

Please replace paragraph [0030] presented in the amended specification dated January 8 2004 with the following original paragraph:

[0030] **Example 6 ~~Example 3~~ L-Se-methylselenocysteine from L-chloroalanine hydrochloride** (using hypophosphorous acid to reduce dimethyldiselenide to methane selenol): In a reaction flask equipped with a stirrer and condenser dimethylformamide (25ml) and dimethyldiselenide (55 g) were taken under an atmosphere of nitrogen. To this solution was added slowly hypophosphorous acid (32% solution, 73g) over a period of 30 mts. The reaction mixture was slowly heated to 70° C and maintained for 2 hrs. The reaction mixture was cooled to 10° C and sodium hydroxide solution (20g in 100 ml water) was added slowly. The mixture was stirred for another 30 mts at that temperature and L-chloroalanine hydrochloride (25 g in 100 ml water) was added over a period of 1 hr. The reaction mixture was stirred for another 1 hr at RT and 1 hr at 40° C. After TLC indicated completion of the reaction, the reaction mixture was worked up as in Example 4. Yield : 10g

Please replace paragraph [0031] presented in the amended specification dated January 8 2004 with the following original paragraph:

[0031] **Example 7 ~~Example 4~~ DL-Se-Methyl selenocysteine**



L-Se-Methylselenocysteine DL-Se-Methylselenocysteine

A single-necked RB flask equipped with a magnetic stirring bar was charged with L-Methyl selenocysteine (0.5g), benzaldehyde(25 mg) and acetic acid (6 ml). The resulting suspension was heated to 60^0C; After 15 minutes the reaction mixture became a clear solution. In another 20 minutes precipitation started. The mixture was stirred at this temperature for 2 hrs, then cooled to room temperature and filtered. The solid material was washed with ethanol thoroughly and dried in vacuo to afford 460 mg of white crystalline solid, DL-Se-MethylselenocysteineYield: 460mg, 92%; MP: 189-190^0C. The chiral HPLC of this material (Figure 1) indicated only two peaks of equal areas attesting to its racemic nature; No other peaks were detected; the peak with lower RT corresponded to L-Methyl selenocysteine.

Please replace paragraph [0032] presented in the amended specification dated January 8 2004 with the following paragraph:

[0032] Convenient processes are described for the synthesis of L-Se-methyselenocysteine from chloroalanine derivatives. Chloroalanine itself is produced in a new method involving Serine methyl ester hydrochloride and thionyl chloride. The process is easily extendable to other selenium substituted amino acids. DL-Se-methylselenocysteine is easily obtained by a benzaldehyde-catalyzed racemization of L-Se-methyselenocysteine.